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Award Number: DAMD17-03-1-0670

TITLE: The Use of a Cognitive Protectant to Help Maintain
Quality of Life and Cognition in Premenopausal Women with
Breast Cancer Undergoing Adjuvant Chemotherapy

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REPORT DATE: October 2004

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

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20050308 051

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE October 2004	3. REPORT TYPE AND DATES COVERED Annual Summary (3 Sep 2003 - 2 Sep 2004)
4. TITLE AND SUBTITLE The Use of a Cognitive Protectant to Help Maintain Quality of Life and Cognition in Premenopausal Women with Breast Cancer Undergoing Adjuvant Chemotherapy			5. FUNDING NUMBERS DAMD17-03-1-0670
6. AUTHOR(S) Jennifer R. Klemp			
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Kansas Medical Center Kansas City, Kansas 66160 <i>E-Mail:</i> jklemp@kumc.edu			8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER
11. SUPPLEMENTARY NOTES			
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) <p>Women undergoing chemotherapy for a diagnosis of breast cancer experience a decrease in quality of life and particularly a reduction in cognitive function, both during and subsequent to therapy. In order to target the quality of life and cognitive function in pre-menopausal women undergoing chemotherapy we are evaluating the effects of chemotherapy on cognitive function, quality of life and fatigue. Pre-menopausal women with breast cancer receiving adjuvant or neoadjuvant chemotherapy including either adriamycin or epirubicin plus cyclophosphamide every two or three weeks are recruited to participate in the study. Evaluations of the study endpoints are done prior to receiving the first cycle, prior to initiating the third cycle, and approximately three weeks after completing the final cycle of chemotherapy, but prior to any additional treatment. Eligible subjects complete a series of self and staff administered tests. The results will be compared with other factors including serum hormone levels, hemoglobin level, neurocognitive markers, symptoms, and whether or not darbepoetin alfa was administered to subjects with a hemoglobin level ≤ 11 g/dL. Results from this study may provide necessary data to support a large scale study examining the role of chemotherapy, cognitive function, and quality of life in breast cancer patients.</p>			
14. SUBJECT TERMS Quality of life, cognition, memory, breast cancer, cognitive protectant			15. NUMBER OF PAGES 5
			16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited

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Introduction:

Significant reduction in cognitive function is observed in 18-50% of women receiving standard dose adjuvant chemotherapy, even several years after treatment. Fatigue is a symptom that can adversely affect neurocognitive function and is reported by approximately 50-85% of women receiving adjuvant chemotherapy. Erythropoietin injections have been shown to improve quality of life and cognition in dialysis patients and are currently used in women receiving chemotherapy and/or radiation with anemia-related symptoms such as fatigue and dyspnea. The administration of erythropoietin to pre and post-menopausal women with breast cancer receiving neo-adjuvant or adjuvant chemotherapy and who had a hemoglobin of <10.5 g/dL, exhibited improved hemoglobin, quality of life, energy and survival relative to placebo. However, in a recent reaction paper published in Lancet Oncology, Leyland-Jones, et al., reported that patients with metastatic breast cancer who participated in a trial using prophylactic erythropoietin, were found to have an increase in adverse events compared to the control group (Leyland-Jones, 2003).

Because of this recent discovery the Federal Drug Administration now prohibits the use of prophylactic erythropoietin in any investigator and industry sponsored clinical trials. As a result, the proposed study design in this application had to be modified to meet current FDA requirement. In order to accommodate the changes recommended by the FDA this study design no longer randomizes subjects between erythropoietin and placebo, but utilizes a within subject design with all subjects receiving erythropoietin once their hemoglobin reaches ≤ 11 g/dL. Although the design has undergone changes, the study question of measuring change in cognitive function and quality of life remains the primary endpoint. The main difference between the initial and revised studies is that the statistical analysis will compare within subject change between baseline, prior to third cycle of chemotherapy and approximately three weeks following completion of the final cycle of chemotherapy.

Key Accomplishments:

- Updated protocol to include new recommendations from the FDA on erythropoietin use.
- Protocol underwent re-review by industry and FDA.
- Validation of psychosocial tools.
- Validation of serum biomarker assays.
- Collaboration with psychologist at Mayo clinic to increase the sensitivity of the main tool to assess cognitive function- High Sensitivity Cognitive Screen.
- Developed recruitment tools and referral basis for this study.
- Protocol and recruitment tools underwent review by KUMC human subjects committee.

Conclusions:

Although modifications to the initial protocol had to incorporate changes brought forth by the FDA, the power and study questions have been maintained. Determining the impact of chemotherapy on cognition and quality of life in young women with breast cancer is important for designing future related studies and providing women with information and tools that may prevent some of the neuro-side effects of chemotherapy.

References:

Leyland-Jones, B. and the BEST Investigators Study Group. Breast cancer trial with erythropoietin terminated unexpectedly. The Lancet Oncology. 4:459-460; 2003.